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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/937,060	04/15/2002	Olga Bandman	PF-0683 USN	4673

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Legal Department
Incyte Genomics
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EXAMINER	
PROUTY, REBECCA E	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 03/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/937,060	BANDMAN ET AL.	
	Examiner	Art Unit	
	Rebecca E. Prouty	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15,17,18,20,21 and 23* is/are pending in the application.

4a) Of the above claim(s) *1,2,7,9,12-15,17,18,20,21 and 23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-6, 8, 10, 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Claims 16, 19, and 22 have been canceled. Claims 1-15, 17, 18, 20, 21, and 23 are still at issue and are present for examination.

Applicants' arguments filed on 12/8/03, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Applicants request to further reconsider the restriction between Group I(E) and elected Group II(E) in view of the amendments to the claims is noted. However, unity of invention is still not present as the two groups do not share a special technical feature as defined under PCT Rule 13.2 as Kohama et al. teach a sphingosine kinase which comprises a sequence identical to amino acids 77-109 of SEQ ID NO:5 (which clearly would be an immunogenic fragment of SEQ ID NO:5) as well as many other fragments of SEQ ID NO:5.

Claims 1, 2, 7, 9, 12-15, 17, 18, 20, 21, and 23 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely

traversed the restriction (election) requirement in the response filed 5/6/03.

This application contains claims 1, 2, 7, 9, 12-15, 17, 18, 20, 21, and 23 drawn to an invention nonelected with traverse in the response filed 5/6/03. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claims 3-6 and 8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The recitation of "has sphingosine kinase activity" in Claim 3 (upon which Claims 4-6 and 8 depend) does not have support in the specification as filed. Applicants point to page 59 of the specification which includes the portion of Table 2 which describes SEQ ID NO:5 as providing support for the instant amendment. However the only mention of sphingosine kinase activity on page 59 (or indeed within the entire specification) is in the column entitled "Homologous Sequences" which page 23

of the specification states shows homologous sequences as identified by BLAST analysis. As such this portion of the specification is merely describing the activity of the **closest homolog not of the polypeptide of SEQ ID NO:5.** This passage does not support the amendment that SEQ ID NO:5 or any fragment thereof has spingosine kinase activity.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 3-6, 8, 10 and 11 remain rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility. The rejection is explained in the previous Office Action.

Applicants state that they "direct the Examiner's attention to those points in the specification that detail the specificity of the claimed polypeptide. In particular, Applicants direct the Examiner's attention to the specification at p. 23, lines 11-18. These lines describe the methods with which the claimed polypeptides are characterized. In particular, column 5 (of Table 2 shows the amino acid residues comprising signature

sequences and motifs; column 6 shows homologous sequences as identified by BLAST analysis and the methods of column 7 were used to characterize each polypeptide through sequence homology and protein motifs." However, it is just this portion of the specification that highlights the fact that the specification **does not assert that the polypeptide of SEQ ID NO:5 has sphingosine kinase activity**. As quoted by applicants column 6 of Table 2 merely describes the closest homolog of the protein of SEQ ID NO:5 as being a sphingosine kinase. Not once does any disclosure of the specification explicitly or implicitly ever state that the protein of SEQ ID NO:5 has this function. In fact only column 5 of this table which is entitled "Signature Sequences" could be considered to even implicitly assert any functional activity of SEQ ID NO:5 (the remaining columns describe strictly structural features of the protein). As the recitation here was to a diacylglycerol catalytic domain, this potential implicit assertion was discussed by the examiner in the previous Office Action. The examiner did not as applicant argues ignore applicants assertion of sphingosine kinase activity because the specification **never made such an assertion.** The only functional assertion made in the specification is the much more general assertion of "kinase activity" which was

discussed in detail in the previous Office Action. In view of the total lack of any assertion in the specification that the protein of SEQ ID NO:5 has sphingosine kinase activity, applicants statements that the post-filing reference of Nava et al. and 80% homology of the mouse homolog cited in Table 2 provides evidence in support of applicants assertion is moot as applicants never made this assertion.

In response to the Examiner's statement that although applicants assert that the claimed polynucleotides are useful for the diagnosis, treatment or prevention of neurological, cell proliferative and autoimmune/inflammatory disorders, there is no link of SEQ ID NO:19 to a specific disease state, applicants state that p. 57 of the specification (Table 1, row 6), column 5 shows a list of specific CDNA libraries in which fragments of SEQ ID NO:19 were expressed, which includes the fragment 1519153H1 which was expressed in a cDNA library derived from bladder tumor tissue. Applicants argue that these data support the assertion that SEQ ID NO:19 may be useful in the diagnosis, treatment or prevention of this cell proliferative disorder by showing that SEQ ID NO:19 is expressed in at least one cell proliferative disorder, i.e., bladder cancer. This argument is not persuasive as the data presented fail to support such an

assertion. There is no evidence of record to show that the expression of this polynucleotide is indicative of bladder cancer or that this polynucleotide and/or the protein it encodes can be used in the treatment or prevention of bladder cancer. Merely because the polynucleotide is expressed in a single bladder cancer tissue does not mean it can be used in the diagnosis or treatment of this disease. Usefulness for diagnosis would require a showing that there is some measurable distinction in the expression of this polynucleotide between cancerous tissue and non-cancerous tissue such that the expression can be correlated to the presence/absence of the disease. No such showing has been made.

Applicants further traverse the instant rejection by arguing that the claimed polynucleotide has utility without requiring knowledge of the function of the encoded polypeptide. Applicants cite two declarations of Dr. Tod Bedilion, a declaration of Dr. John Rockett and a declaration of Dr. Vishwanth Iyer, all filed December 8, 2003 in support of their argument and assert that these declarations demonstrate the utility rejection is without merit. Applicants assert the first Bedilion Declaration describes how the claimed polynucleotide can be used in gene expression monitoring systems that were

allegedly well known at the time of the invention, and how those applications are useful in developing drugs and monitoring their activity. Applicants assert that the law has never required knowledge of biological function to prove utility and further assert the uses of the polynucleotide in gene expression monitoring applications are independent of its biological function. Applicants' argument is not found persuasive.

It is noted that Dr. Tod Bedilion is a consultant for Incyte Corporation and thus is a concerned party. Regarding the merit of the examiner's position, *any* polynucleotide can be used for gene expression monitoring and consequently, this asserted utility is **not** specific. Furthermore, the specification fails to provide guidance as to enable a skilled artisan to use data relating to the claimed polynucleotides derived from the results of toxicology testing and what the results would mean. For example, if the claimed polynucleotide was attached to a microarray and used in toxicology testing or gene expression analysis and a result showed that expression was increased when a cell was treated with a particular agent, the specification provides no basis on which a skilled worker would be able to determine whether that result is meaningful. As such, further experimentation would be required to interpret the results of

such gene expression analysis and consequently, this asserted utility is *not* substantial. The examiner acknowledges that the utility requirement does not require knowledge of biological function. A claimed polynucleotide can meet the requirements of utility as long as the specification discloses a credible, specific and substantial asserted utility or a well-established utility for the claimed polynucleotide, even though the function of the polynucleotide or encoded polypeptide is not disclosed in the specification. For example, Shattuck-Eidens et al. (US Patent 5,693,473) teach mutant alleles of the *BRCA1* gene that predispose a patient to developing breast and ovarian cancers (abstract). While there is no disclosure of the function of the mutant *BRCA1* genes or their gene products, the invention nevertheless has utility as being an indicator for susceptibility to developing breast and ovarian cancers. Contrary to this example, the instant specification fails to assert a specific and substantial utility for the claimed polynucleotide.

Applicants argue that in order to satisfy the utility requirement of 35 USC 101 and 112, first paragraph, the applicant need only show that the invention is "practically useful" and confers a "substantial", "specific benefit" on the

public. Applicants cite the following case law that is allegedly relevant to the instant rejection: *Anderson v Natta*, 480 F.2d 1392, 1397, 178 USPQ 458 (CCPA 1973); *Brenner v Manson*, 383 US 519, 534-35, 148 USPQ 689 (1966); *Juicy Whip Inc. v Orange Bang Inc.*, 51 USPQ2d 1700 (Fed Cir 1999); *Stiftung v Renishaw PLC*, 945 F2d 1173, 1180, 20 USPQ2d 1094 (Fed Cir 1991); *Standard Oil Co. v Montedison, S.p.a.*, 212 USPQ 327 343 (3d Cir 1981); *Cross v Izuka*, 753 F2d 1040, 1048 (Fed Cir 1985); *Nelson v Bowler*, 626 F2d 853, 856, 206 USPQ 881 (CCPA 1980); *In re Cortright*, 165 F3d 1353, 1357, 49 USPQ2d 1464 (Fed Cir 1999); *In re Brana*, 51 F3d 1560, 1566; 34 USPQ2d 1436 (Fed Cir 1995); and *In re Langer*, 503 F2d 1380, 1391-92, 183 USPQ 288 (CCPA 1974). Applicants' argument is not found persuasive. The essential disagreement between the examiner's position and applicants' position appears to be the interpretation of what constitutes a specific and substantial utility, as will be explained in detail below.

Applicants argue the claimed invention meets all necessary requirements for establishing a credible utility under the law as there are allegedly "well-established" uses for the claimed invention and there are allegedly specific practical and beneficial uses disclosed in the specification for the claimed invention as disclosed in the first Bedilion Declaration and

that objective evidence, allegedly not considered by the Office, further corroborates the credibility of the asserted utilities. Applicants' argument is not found persuasive.

The claimed invention has no well-established use and there is no specific and substantial use for the claimed invention. Each of applicants' asserted utilities for the claimed polynucleotide, *i.e.*, diagnosis of conditions and disorders characterized by expression of polynucleotides encoding SEQ ID NO:5, for toxicology testing, and for drug discovery, will be addressed in detail below. Applicants do not elaborate on the "objective evidence" that has allegedly not been considered by the Office. Contrary to applicants' assertion, the examiner has fully considered ALL evidence of record in evaluating the claims for utility under 35 USC §§ 101 and 112, first paragraph.

Applicants argue the claimed invention has real-world utility as allegedly being useful for toxicology testing, drug development, and disease diagnosis through gene expression profiling, allegedly explained in the first Bedilion Declaration, the substance of which is allegedly not rebutted by the Examiner. Applicants argue there is no dispute that the claimed invention is a useful tool in cDNA microarrays used to perform gene expression analysis. Applicants assert that these

uses are sufficient to establish utility for the claimed polynucleotide. Applicants argue the Bedilion Declaration explains the many reasons why a person skilled in the art reading the instant application would have understood this application to disclose the claimed polynucleotide to be useful for a number of gene expression monitoring applications, such as a probe for expression of the polynucleotide in connection with the development of drugs and the monitoring of the activity of such drugs. Applicants argue the examiner does not address the "fact" that the claimed polynucleotide can be used as highly specific probes to measure both the existence and amount of complementary mRNA sequences known to be expression products of the claimed polynucleotide. Applicants argue that the claimed invention is not some random sequence whose value as a probe is speculative or would require further research to determine. Applicants' arguments are not found persuasive.

It should be noted that the Bedilion Declaration has only been made of record with the amendment filed December 8, 2003 and therefore, the examiner has not had the opportunity to rebut the statements provided therein. The examiner agrees with the Bedilion Declaration (and those of Drs. Rockett and Iyer as well) to the extent that *any* polynucleotide, including the

claimed polynucleotide, can be included as part of a cDNA microarray, however, this use does not confer patentable utility on the claimed polynucleotide as this utility is considered a general use and not a utility that is specific and substantial. MPEP § 2107.01 states, "A 'specific utility' is *specific* to the subject matter claimed. This contrasts with a *general* utility that would be applicable to the broad class of the invention". Expressed polynucleotides have a variety of general uses, *e.g.*, as a probe for hybridization or as a template for protein expression - these uses are applicable to *any* expressed polynucleotide and are not specific to the claimed polynucleotide. Also, the claimed polynucleotide has no substantial utility. MPEP § 2107.01 states, "Utilities that require or constitute carrying out further research to identify or reasonably confirm a 'real world' context of use are not substantial utilities". Because the specification fails to provide guidance to allow a skilled artisan to use data relating to the **claimed** polynucleotide derived from the results of gene expression analysis and what the results would mean, the results of gene expression monitoring assays would be meaningless without further research. In this case, the asserted use of the claimed polynucleotide for gene expression monitoring would be

an assay to measure a polynucleotide that itself has no specific and substantial utility. MPEP § 2107.01 states that this utility is *not* substantial: "A method of assaying for or identifying a material that itself has no specific and/or substantial utility". Consequently, the claimed polynucleotide has no specific and substantial utility.

Applicants argue that because the claimed polynucleotide is expressed, its utility as a measuring and analyzing instrument for expression levels is as indisputable as a scale's utility for measuring weight. Applicants cite case law as allegedly relevant to the patentable utility of research tools.

It is true that a scale, gas chromatograph, screening assays, and nucleotide sequencing techniques have utility as research tools. However, such tools present a result that requires no further experimentation for interpretation, *e.g.*, a scale provides the weight of an object and requires no further experimentation for interpretation of the result. In the instant case, a more representative analogy to the claimed polynucleotide would be that of a scale without an identifiable unit of measure - one could place an object on the scale, however, further experimentation would be required to interpret the result and determine the weight of the object. Similarly, as

applicants have provided no information regarding altered expression of the claimed polynucleotide or guidance for interpreting the results of gene expression analysis, additional experimentation would be required to interpret a result obtained using the claimed polynucleotide for gene expression analysis.

There is no evidence of record to suggest that the claimed polynucleotide has ANY association with ANY disease state. Applicants are invited to provide such evidence. However, in view of the lack of such evidence, such an association between the claimed polynucleotide and any disease states, for example bladder cancer, does not exist. As stated above, any polynucleotide can be used for gene expression analysis and the specification fails to provide guidance to allow a skilled artisan to use information relating to the claimed polynucleotide derived from the results of gene expression analysis and what the results would mean, the results of gene expression monitoring assays using a cDNA microarray comprising the claimed polynucleotide would be meaningless without further research. In this case, the asserted use of the claimed polynucleotide for gene expression monitoring would be an assay to measure a polynucleotide that itself has no specific and substantial utility. MPEP § 2107.01 states that this utility is

not substantial: "A method of assaying for or identifying a material that itself has no specific and/or substantial utility". Consequently, the claimed polynucleotide has no specific and substantial utility.

Applicants refer to Dr. Bedilion's opinionated discussion of Brown et al. (US Patent 5,807,522, cited by applicants). Dr. Bedilion characterizes the patent as providing evidence that microarrays can be used in numerous genetic applications, including monitoring of gene expression in different tissue types, disease states, in response to drugs, and in response to potential toxins. Applicants also cite the references of Rockett et al. (*Xenobiotica* 29:655) and Lashkari et al. (*Proc Natl Acad Sci* 94:8945-8947) as allegedly describing the use and importance of gene expression technology with respect to drug screening and toxicology testing. Applicants' arguments are not found persuasive.

The claims of the Brown et al. patent are drawn to methods of forming microarrays (see, for example, claim 1 of Brown et al.). Methods of forming a microarray have patentable utility. However, in the instant case, a microarray comprising the claimed polynucleotide does not have patentable utility as stated in detail above. Applicants' arguments and alleged

supporting evidence merely indicate that microarray technology is important and useful to the scientific community. These publications are unrelated to the claimed polynucleotide and fail to demonstrate the claimed invention has *any* patentable utility. The use of the claimed and functionally uncharacterized polynucleotide in such studies would provide no more information than the use of any other uncharacterized polynucleotide. The asserted utility for the claimed polynucleotide is not specific to the claimed polynucleotide as stated above. Furthermore, due to the lack of disclosure of a correlation between the claimed polynucleotide and a particular disorder or guidance for interpreting the data obtained from gene expression analysis, the asserted utility is also not substantial, as discussed in detail above.

Applicants argue the claimed polynucleotides are useful as tools for toxicology testing, drug discovery, and the diagnosis of disease and that these uses are "well-established". Applicants cite the references of Rockett et al. (*Xenobiotica* 29:655), Lashkari et al (*PNAS 94 :8945-8947)*, Nuwaysir et al. (*Mol Carcinogen* I24 :153-159), Steiner et al. (*Tox Lett* 13 :467-471), Rockett et al. (*Environ Health Perspectives* 107:681), US Patent 5,569,588, published PCT applications WO 95/21944, WO

95/20681, and WO 97/13877, an email from Dr. Cynthia Afshari to an Incyte employee, and examples (as set forth at the bottom of page 29 of the response filed December 8, 2003) that allegedly support applicants' assertions. Applicants argue that, because the examiner has allegedly failed to address or consider the "well-established" utilities for the claimed invention in toxicology testing, drug development, and disease diagnosis, the rejections should be withdrawn. Applicants' arguments are not found persuasive.

Each of these uses (toxicology testing, drug development, and disease diagnosis) will be addressed individually, because the facts and issues directed to each use are distinct and separable. First, applicants argue that toxicology testing is a well-established utility and concludes that the claimed polynucleotides could be used in this manner and that the claimed invention therefore possesses patentable utility. However, for a utility to be "well-established" it must be specific, substantial and credible. In this case all expressed polynucleotides have use in gene expression monitoring for toxicology testing and consequently, this utility is not specific. Furthermore, the specification fails to disclose the methods and information necessary for a skilled artisan to use

the **claimed** polynucleotide for toxicology testing, *e.g.*, how would one interpret the results obtained from such testing? Therefore, this is a utility that would apply to virtually every member of a general class of materials, such as any collection of expressed polynucleotides. Such a utility is **not** specific and does *not* constitute a "well-established" utility. Moreover, use of the claimed polynucleotide in an array for toxicology screening is only useful in the sense that the information that is gleaned from the array is dependent on the pattern derived from the array, and says nothing with regard to each individual member of the array. Again, this is a utility that would apply to virtually every member of a general class of materials, such as any collection of polynucleotides. Even assuming *arguendo* that the expression of applicants' claimed polynucleotide was affected by a test compound in an array for drug screening, the specification does not disclose any guidance for interpretation of the result, and none is known in the art. Given this consideration, the claimed polynucleotide has no "well-established" use. The artisan is required to perform further experimentation on the claimed material itself in order to determine to what "use" any expression information generated using this nucleic acid may have.

With regard to drug discovery and development, applicants mention gene expression profiling as one use of the claimed polynucleotide. Applicants refer to recent developments as providing evidence that the benefits of this information are already beginning to manifest themselves. However, applicants are incorrect in asserting that the efficacy (ability to produce a desired effect) of a compound could be evaluated from the result of a transcript image because there is no way to assess the meaning of any individual "hit" obtained from this procedure. The first requirement is that one must know the biological significance of the polynucleotide(s) which is/are being evaluated. Without this information, the results of the transcript image are useless because one would not inherently recognize how to interpret the result of increased or decreased polynucleotide expression or even what significance could be attributed to such changes in expression profiles. As such information has not been provided in the specification, further experimentation is required to identify a "real world" use for the claimed polynucleotide.

With regard to diagnosis of disease, in order for a polynucleotide to be useful, as asserted, for diagnosis of a disease, there must be a well-established or disclosed

correlation or relationship between the claimed polynucleotide and a disease or disorder. The presence of a polynucleotide in tissue that is derived from normal or cancerous cells is not sufficient for establishing a utility in diagnosis of disease in the absence of some information regarding a correlative or causal relationship between the expression of the claimed polynucleotide and the disease. If a molecule is to be used as a surrogate for a disease state, some disease state must be specifically associated in some way with the molecule. In the absence of any disclosed relationship between the claimed polynucleotides or encoded proteins and any disease or disorder and the lack of any correlation between the claimed polynucleotides or the encoded proteins with any known disease or disorder, any information obtained from an expression profile would only serve as the basis for further research on the observation itself.

Applicants further argue that the utility of the claimed polynucleotide can be imputed based on the relationship between the polypeptide it encodes, HRIP, and another polypeptide of unquestioned utility, sphingosine kinase (see pages 30-31 of applicant's response). While the examiner agrees that the level of identity of the protein of SEQ ID NO:5 to the mosue

sphingosine kinase of Kohama et al. and the human sphingosine kinase of Nava et al. would have supported an assertion of sphingosine kinase activity, this assertion was not made in the application as filed. Disclosure of a patentable use for the claimed invention must be present in the application **as filed.** While post filing evidence may be used to corroborate and support an assertion of utility, the initial assertion must be present in the application as filed. In this case the application as filed is completely lacking any assertion that the protein of SEQ ID NO:5 has sphingosine kinase activity.

Applicants argue that a "real-world" utility exists if actual use or commercial success can be shown. Citing case law, applicants state that such a showing of actual use or commercial success is conclusive proof of utility. Applicants argue that a vibrant market has developed for databases containing all expressed genes, including those of Incyte, the real party at interest. Applicants state Incyte's customers and the scientific community have acknowledged that Incyte's databases have proven valuable, and that the databases including the claimed polynucleotide would be even more valuable. Applicants' arguments are not found persuasive.

The case law indicates that a rejection under 35 U.S.C. § 101 *for lack of operability* can be overcome by a showing of actual use or commercial success. The instant issue is whether or not the asserted utilities meet the three-pronged test for credibility, specificity, and substantiality. Such is not necessarily addressed by a showing of commercial success or actual use. Many products that lack patentable utility enjoy commercial success, are used, and are considered valuable, *e.g.*, a pet rock. In this case, applicants' asserted utilities are neither substantial or specific. Furthermore, while applicants present evidence showing that the database is commercially valuable, there is no evidence to suggest that the database is any more or less valuable with the inclusion of the *claimed* polynucleotide.

Applicants argue that, rather than responding to the evidence allegedly demonstrating utility, the examiner attempts to dismiss it altogether by arguing that the disclosed and well-established utilities for the clamed polynucleotides are not "specific and substantial asserted" utilities. Applicants argue the examiner is incorrect both as a matter of law and as a matter of fact. Applicants' arguments are not found persuasive.

It is the examiner's position that the claimed invention has no well-established use and there is no specific or substantial use for the claimed invention, even after FULL consideration of the "evidence" as provided in the specification. Applicants' arguments will be addressed in detail below.

Applicants argue that the examiner's rejection is based on the grounds that, without information as to the biological role of the claimed polynucleotide, the claimed invention lacks specific patentable utility. Applicants argue that, according to the examiner applicants are required to provide a specific and substantial interpretation of the results generated in an expression analysis. Applicants argue that specific and substantial interpretations regarding biological function are not necessary for obtaining a US patent. Applicants state the relevant question is not how or why the invention works, but whether the invention provides an "identifiable benefit" in currently available form. Applicants argue that the present invention meets this test. Applicants argue that the threshold for patentable utility is low and that only throwaway utilities are insufficient. Applicants' arguments are not found persuasive.

It is noted that applicants' arguments have mischaracterized the examiner's position. The examiner has fully considered applicants' "evidence" allegedly demonstrating utility and, in accordance with 35 USC § 101 has determined the claimed invention to lack patentable utility as the asserted utilities are neither specific nor substantial. The rejection never states that the precise biological role of a polynucleotide is required for it to possess patentable utility. The examiner acknowledges applicants' assertion that biological function of a polynucleotide need not be disclosed for a claimed polynucleotide to have patentable utility (see the example of Shattuck-Eidens et al. in US Patent 5,693,473 as described above). However, the specification fails to provide sufficient guidance such that one of ordinary skill in the art can use the claimed polynucleotide as a disease marker or for toxicology testing, drug discovery, or disease diagnosis and as such, there is no specific and substantial asserted utility. For example, if the claimed polynucleotide were used in a microarray for toxicology testing and if a compound caused the claimed polynucleotide to be expressed at a decreased level as demonstrated by the data generated using the microarray, what information does this provide, other than to initiate further

experimentation? In view of the specification, a skilled artisan would recognize that the determination of whether a compound is potentially therapeutic or deleterious requires significant further research, and thus the asserted utility is not substantial. Also, *any* expressed polynucleotide *can* be used in a microarray - just as any polynucleotide can be used for protein expression and thus the asserted utility is also not specific.

Applicants allege the examiner has refused to impute the utility of the members of the kinase family of proteins to SEQ ID NO:5. Applicants argue the examiner takes the position that utility of the claimed polynucleotide cannot be imputed unless applicants identify which particular biological function within the class of kinases is possessed by SEQ ID NO:5. Applicants argue the examiner would require that all kinases possess a "common" utility in order to demonstrate utility by membership in a class. Applicants state the case law requires only that the class not contain a substantial number of useless members. Applicants argue the examiner has treated the claimed polynucleotide as if it was in a general class of all polynucleotides, rather than the encoding a kinase proteins. Applicants argue the examiner has not presented any evidence that the kinase family of proteins has any, let alone a

substantial number, of useless members. Applicants argue that even if the examiner's common utility criterion were correct, the kinase family would meet it as members of the kinase family are all known to phosphorylate proteins and thus a skilled artisan would not need to know any more than this in order to use the protein encoded by the claimed polynucleotides and the Office action presents no evidence to the contrary. Applicants argue that knowledge that SEQ ID NO:5 is a kinase is sufficient to make it useful for diagnosis and treatment of neurological, cell proliferative, and autoimmune/inflammatory disorders. Applicants argue SEQ ID NO:5 has been shown to be expressed in tissues associated with cancer or inflammation. Applicants conclude that these facts must be accepted as true in the absence of evidence or sound scientific reasoning to the contrary. Applicants' arguments are not found persuasive.

This is not persuasive, while it is agreed that applicants have asserted that the protein encoded by the claimed polynucleotides is a member of the kinase family, as discussed in the previous Office Action, placement of a protein into this family is not sufficient to provide a patentable utility as the skilled artisan would still not know what to do with it without more specific information as to what it phosphorylates. Such

information was not provided within the instant specification. Applicants statement that the kinase family are all known to phosphorylate proteins is in fact completely false. Kinases phosphorylate many types of compounds of which only some are proteins. In fact all available evidence suggests that the instant kinase does not in fact phosphorylate a protein, but instead a lipid (i.e., sphingosine). Other kinases phosphorylate carbohydrates, nucleic acids, and many other small organic compounds within biological systems. While it is true that some kinases are known to be involved in cell proliferative and inflammatory disorders, not all kinases have any role in these processes and there is no evidence of record that the claimed polynucleotide is involved in ANY disease state and it is just as likely that it is not. In view of the failure of the specification to provide a correlation of the claimed polynucleotide to a specific disease state and the necessary guidance for using the claimed polynucleotide to diagnose and treat a specific disorder, significant further research would be necessary for the skilled artisan to use the claimed polynucleotides in a real world context, and thus the asserted utility is not substantial.

Applicants argue the rejection is incorrectly based on the grounds that the use of an invention as a tool for research is not a substantial use. Applicants state that only a limited subset of research uses are not substantial: those in which the only known use for the claimed invention is to be an object of further study, thus merely inviting further research. Applicants argue that nowhere in their cited case law is it stated or implied that a material cannot be patentable if it has some other, additional beneficial use in research. Applicants argue the claimed invention has a beneficial use in toxicology testing, drug discovery, and disease diagnosis. Applicants argue the claimed polynucleotide is a tool not an object of research. Applicants argue the data generated as a result of gene expression monitoring using the claimed invention is not merely to study the polynucleotide itself, but to study properties of tissues, cells, and potential drug candidates and toxins. Applicants argue that without the claimed invention, information regarding properties of tissues, cells, and potential drug candidates and toxins is less complete. Applicants argue the invention has numerous additional uses as a research tool including diagnostic assays, chromosomal markers, ligand screening assays and drug screening.

As discussed above, whereas a scale or gas chromatograph has patentable utility as a research tool as providing a result that can be readily used and provides a specific benefit in currently available form, in this case, the claimed polynucleotide does NOT provide a specific benefit in currently available form and the asserted uses of the claimed polynucleotide either apply to the general class of polynucleotides (chromosomal marker) and/or would require further experimentation as described above (diagnostic assay, ligand screening assay, and drug screening). The claimed polynucleotide is not disclosed as having a property that can be identifiably and specifically useful without further, additional experimentation. The claimed invention is, in fact, the object of further study, merely inviting further research. For example, the specification provides no guidance to allow a skilled artisan to use data relating to the claimed polynucleotide derived from the results of toxicology testing and what the results would mean. For example, if the claimed polynucleotides were attached to a microarray and used in toxicology testing or gene expression analysis and a result showed that expression was increased when a cell was treated with a particular agent, the specification provides no basis on which a skilled worker would

be able to determine whether that result is meaningful. As such, further experimentation would be required to interpret the results of such gene expression analysis. Contrary to applicants' assertions, none of the asserted utilities for the claimed polynucleotide is specific and substantial.

Applicants challenge the legality of the Patent Examination Utility Guidelines. Applicants argue that "unique" or "particular" utilities have never been required by the law and applicants are unaware of any court that has rejected an assertion of utility on the grounds that it is not "particular" or "unique" to the specific invention. Applicants argue that to meet the utility requirement, the invention need only by "practically useful" and confer a "specific benefit" on the public. Applicants' arguments are not found persuasive.

Regarding the Training Materials, applicants are reminded that the examiner must examine a patent application according to the guidelines set forth by the USPTO as well as the MPEP, since the examiner has no authority to disregard such guidelines or to apply his own interpretation of patent law in the examination of the application. Furthermore, as set forth in the guidelines and the MPEP, the guidelines were promulgated by the Patent Office in accordance with all applicable case law and thus are believed

to be consistent therewith. Applicants are further reminded that the examiner has no authority to comment in regard to the legality of the new utility guidelines or the MPEP as set forth by the USPTO. Accordingly, it is the examiner's position that the instant claims, based on an analysis of the utility requirement of 35 USC § 101 and following the current Utility Guidelines, have no specific, substantial, or credible utility.

Regarding applicants' comments regarding a "unique" utility, it is noted that applicants' characterization of the examiner's position is somewhat misleading. Applicants have never been asked to identify a utility that is unique, i.e., not shared by any other compounds or compositions. Rather, applicants have been required to identify a utility that is specific to the invention claimed, as opposed to one that would apply regardless of the specific properties of the claimed invention. An invention certainly can have a utility that is shared by other compounds or compositions. While a utility need not be unique to a claimed invention, it must nonetheless be specific, and in currently available form, in order to satisfy 35 USC § 101.

Claims 3-6, 8, 10, and 11 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention

is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Even if applicants show that a polynucleotide encoding the protein of SEQ ID NO:5 has a patentable utility, the following scope of enablement rejection would still apply.

Claims 3, 5, 6, 8, 10 and 11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for polynucleotides encoding SEQ ID NO:5, does not reasonably provide enablement for polynucleotides encoding any naturally occurring protein which is 90% identical to SEQ ID NO:5 or comprising an immunologically active fragment of SEQ ID NO:5 or any DNA which is 90% identical to SEQ ID NO:19 or comprises a fragment of at least 500 nucleotides of SEQ ID NO:19. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The rejection is explained in the previous Office Action.

It is the examiner's position that the specification, while being enabling for a polynucleotide encoding SEQ ID NO:5 and a

microarray comprising said polynucleotide, does not reasonably provide enablement for the entire scope of claimed polynucleotides and microarrays. Applicants argue that one of skill in the art can readily identify the entire scope of claimed polynucleotide variants using known methods without undue experimentation. Applicants argue a skilled artisan would know how to use the entire scope of claimed variants. Applicants argue that one need only screen naturally occurring variants that have been determined through natural selection. Applicants argue the claims are drawn to polynucleotides and not polypeptides and it is the functionality of the polynucleotides that is relevant. Applicants argue that even nucleic acids encoding defective polypeptides may be useful. Applicants argue the examiner has failed to provide any reasons why one would doubt the guidance provided by the specification would enable one to make and use the claimed invention without undue experimentation according to the "standard" set forth in *In re Marzocchi*, 169 USPQ 367, 369 (CCPA 1971) and *In re Borkowski*, 164 USPQ 642, 645 (CCPA 1970) and has not established a *prima facie* case of non-enablement. Applicant's arguments are not found persuasive.

Contrary to applicant's assertion, the examiner provided numerous reasons why applicant has not enabled the entire scope of claimed invention - see the analysis set forth in the Office action mailed June 4, 2003. While methods of isolating naturally-occurring variants of a given sequence are known in the art, *e.g.*, hybridization, the specification fails to provide guidance for **using** the entire scope of claimed nucleic acids. In this case, the claims encompass a broad scope of nucleic acids encoding polypeptides having *any* function. The specification fails to provide guidance for making and using these variants. While applicants have limited the claims to naturally-occurring variants, it is well known in the art that it is unpredictable that two naturally-occurring polypeptides (even those that are highly structurally similar) will necessarily share similar function. In fact the frequent occurrence of non-functional allelic variants of many genes is clear evidence that one can not predict function merely from structural similarity as alleles are highly structurally similar, yet often very different functionally. Furthermore, the art provides other examples of polypeptides have structural similarity, yet differ functionally. See for, example Seffernick et al. who teach two polypeptides that share 98% amino acid sequence identity (99%

nucleic acid sequence identity) with distinct functions. This degree of unpredictability is greatly increased when one considers that the claimed variants broadly encompass those that are 90% identical to SEQ ID NO:5 or SEQ ID NO:19. Furthermore, contrary to applicants' assertion, the specification fails to provide guidance for using those polypeptides encoded by nucleic acids that are non-functional. While the claimed nucleic acid *may* useful in diagnosing one or more of the hundreds of diseases set forth in the specification, the specification fails to provide specific guidance for treating or diagnosing ANY specific disease. Thus, an undue amount of experimentation would be required to first determine whether any of the polynucleotide variants encompassed by the claims are causative or associated with any of the hundreds of diseases listed and further experimentation would be required to determine the steps required to diagnose or treat those disease states – if any. In this case, applicants would require that a skilled artisan perform significant further experimentation without a particular direction to make and use the claimed variants. It is noted that nowhere does the examiner state that the claimed polynucleotide must encode a functional polypeptide. However, the specification clearly does not teach how a skilled artisan is use the entire

scope of claimed polynucleotides, including those that encode non-functional polypeptides. Instead, the specification teaches only a single working example of the claimed polynucleotide – SEQ ID NO:19 and a single working example of the claimed polypeptide – SEQ ID NO:5. The specification provides no further guidance for using those polynucleotides that encode non-functional polypeptides or those polypeptides having function other than sphingosine kinase activity. At most the specification provides a description that will enable a skilled artisan to *attempt to discover* how to make and use the claimed invention and provides no more than a starting point for significant further experimentation (see *University of Rochester v. G.D. Searle & Co. Inc.*, W.D. N.Y., No. 00-CV-6161L, 3/5/03).

Claims 3, 5, 6, 8, 10 and 11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is explained in the previous Office Action.

It is the examiner's position that the claimed genera of polynucleotides and microarrays are not adequately described in

the specification. Applicants argue the claimed subject matter is either disclosed or is conventional or well known to a skilled artisan. Applicants provide alleged support for the variants and fragments as encompassed by the claims. Applicants argue that a skilled artisan would recognize polypeptide sequences that are naturally occurring variants that are at least 90% identical to a nucleic acid encoding SEQ ID NO:5 or the nucleic acid of SEQ ID NO:19. Applicants argue that given a naturally occurring polynucleotide sequence, it would be routine for a skilled artisan to recognize whether it is a variant of a nucleic acid encoding SEQ ID NO:5 or the nucleic acid of SEQ ID NO:19. Based on this alleged "routine recognition", applicant concludes that the specification provides an adequate description of the claimed variants of a nucleic acid encoding SEQ ID NO:5 or the nucleic acid of SEQ ID NO:19. Applicant's argument is not found persuasive.

The specification provides only *a single representative species* of the claimed genus of polynucleotides, *i.e.*, SEQ ID NO:19. For claims drawn to a genus, MPEP § 2163 states the written description requirement for a claimed genus may be satisfied through sufficient description of a *representative number of species* by actual reduction to practice, reduction to

drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406. MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. Other than the *single representative species* as described above, the specification fails to describe any additional representative species of the claimed genus. While MPEP § 2163 acknowledges that in certain situations "one species adequately supports a genus", it is also acknowledges that "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus". In the instant case, the claimed genus of polynucleotides encompasses species that bind to polypeptides

that are widely variant in both structure and function, including (but not limited to) functional and non-functional allelic variants and polypeptides having function other than sphingosine kinase. As such, the disclosure of the single representative species of SEQ ID NO:19 is insufficient to be representative of the attributes and features of *all* species encompassed by the claimed genus. Applicant's alleged supporting description of variants of a nucleic acid encoding SEQ ID NO:5 or the nucleic acid of SEQ ID NO:19 merely provides a textual description of said variants without providing any structural or functional features of the species encompassed by the genus. As such, a skilled artisan would *not* be able to visualize the structure of each member of the claimed genus. Furthermore, because there is no functional limitation provided for the variants of a nucleic acid encoding SEQ ID NO:5 or the nucleic acid of SEQ ID NO:19, one of skill in the art would recognize that the claimed genus of variants encompasses species having substantial variation of function within the genus. One of skill in the art would recognize that such variants encompass polypeptides having *any* activity, including non-functional polypeptides and polypeptides having a function other than sphingosine kinase. When there is substantial variation within a

genus, as is the instant case, one must describe a sufficient variety of species to reflect the variation within the genus. The single representative species of SEQ ID NO:19fails to describe the entire genus of claimed polynucleotides.

Applicant summarizes case law citing *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed Cir 1993) and *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (Fed Cir 1997) as court cases in which the recitation of functional characteristics of a DNA, without description of structural features has been a basis by which the courts have found invalid claims to DNA. Applicant argues the claims at issue are in contrast to the claims of the *Lilly* and *Fiers* cases as applicant alleges the claimed genus of polynucleotides is defined by structure rather than function. Applicant argues there is no reliance solely on functional characteristics of the claimed polynucleotides. Applicant argues the Office has failed to base the written description inquiry "on whatever is now claimed" and fails to provide an appropriate analysis of the instant claims and how they differ from those of the *Lilly* and *Fiers* cases. Applicant's arguments are not found persuasive.

While it is acknowledged that the current claims differ from those of the *Lilly* and *Fiers* cases, as discussed in the

written description Guidelines and MPEP § 2163, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show applicants were in possession of the claimed genus. A representative number of species means that the species that are adequately described are representative of the entire genus. The specification discloses only a single representative species of the claimed genus of claimed polynucleotides, i.e., SEQ ID NO:19 a. Furthermore, as stated above, there is substantial variation within the structure AND function of the genus of claimed polynucleotides. When there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. At the time of the invention, one of skill in the art would recognize the absence of the ability to predict the function(s) of all species of polynucleotides encompassed by the genus. For inventions in an

unpredictable art, adequate written description of a genus that embraces widely variant species cannot be achieved by disclosing only one species within the genus. As described above, one of skill in the art would recognize that the genus of variants of a nucleic acid encoding SEQ ID NO:5 or the nucleic acid of SEQ ID NO:19 encompasses species having *substantial* variation of both structural AND functional features. As such, neither the description of the structure and function of SEQ ID NO:19 nor the disclosure of solely structural features present in all members of the genus is sufficient to be representative of the attributes and features of the entire genus of claimed polynucleotide.

Applicants argue the claims do not describe a genus that is highly variant. Applicant argues that available evidence indicates that the claimed genus is of narrow scope. In support of applicant's assertion, they rely on the teachings of Brenner et al. (*Proc Natl Acad Sci USA* 95:6073-6078; cited by applicant). Applicants argue that, based on the teachings of Brenner et al., naturally-occurring molecules may exist that could be characterized as kinases with only 40% identity over 70 amino acid residues of SEQ ID NO:5. Applicant argues the claims recite, e.g., a naturally occurring polynucleotide encoding an

amino acid sequence with at least 90% identity to SEQ ID NO:5, which has 384 amino acids. Applicant asserts this variation is far less than those kinases having as little as 40% identity over 70 residues of SEQ ID NO:5. Applicants' argument is not found persuasive.

Applicant improperly attempts to apply the teachings of Brenner et al. (*Proc Natl Acad Sci USA* 95:6073-6078) to support their argument. Brenner et al. (*Proc Natl Acad Sci USA* 95:6073-6078) clearly state that their comparisons "have been assessed using proteins whose relationships are known reliably from their [three dimensional] structures and functions, as described in the SCOP database" (page 6073, abstract). Murzin et al. (*J Mol Biol* 247:536-540) teach that the proteins of the SCOP database have been characterized both in their three dimensional structures AND their function. In the instant case, there is no evidence of record that would indicate that the polypeptide of SEQ ID NO:5 has been characterized by either of these methods. In fact, the function of the polypeptide of SEQ ID NO:5 appears to have been assigned based solely on its amino acid sequence - not on its three dimensional structure or its alleged kinase function. The specification provides no disclosure of the three dimensional structure of the polypeptide of SEQ ID NO:5 or an

empirical activity assay such that the teachings of Brenner et al. (*Proc Natl Acad Sci USA* 95:6073-6078) could be applied to the polypeptide of SEQ ID NO:5. Brenner et al. (*Proc Natl Acad Sci USA* 95:6073-6078) compare amino acid sequences of polypeptides whose functions have been empirically characterized that are encoded by genes at *different* loci and suggest that 30 % sequence identity between polypeptides having the aforementioned characteristics, i.e., functional polypeptides encoded by genes at different loci, can be used to propose functional similarity of the polypeptides. However, Brenner et al. (*Proc Natl Acad Sci USA* 95:6073-6078) clearly DOES NOT suggest that *all* amino acid sequences with at least 40 % identity over 75 amino acids to another amino acid sequence will share a similar function. Instead, Brenner (*Trends in Genetics* 15:132-133) discloses his opinion of functional prediction of a polypeptide *based solely on amino acid sequence* by teaching that it is impossible to know the accuracy of functional assignment without empirical laboratory evidence (page 132, left column, second paragraph), which it is noted, has not been provided in the specification. Also, it is well known in the art that highly homologous proteins can have distinct functions. As supporting evidence, the examiner provides the reference of Scott et al.

(*Nat Genet* 21:440-443) who state that their result shows the importance of confirming the function of a protein even when the protein shares significant homology to proteins of known function (page 441, left column, third full paragraph). It is noted that applicant's claims are drawn to naturally occurring polynucleotides and polypeptides. The examiner provides the reference of Seffernick et al. (*J Bacteriol* 183:2405-2410) who teach two polypeptides having distinct functions that share 98% amino acid sequence identity (page 2407, right column, middle). While Seffernick et al. characterize their finding as "exceptional" (page 2409, left column, middle), this nonetheless provides evidence that polypeptides, even those sharing significant sequence identity, do not necessarily share function as asserted by applicant.

Applicants argue the state of the art at the time of the invention is further advanced than at the time of the *Lilly* and *Fiers* cases. Applicant argues the techniques and technological advances since the *Lilly* and *Fiers* cases up to the filing of the instant application in combination with the teachings provided in the instant specification are such that one of skill in the art would recognize that applicant was in possession of the

claimed polynucleotides. Applicant's arguments are not found persuasive.

While advances in the art are undeniable and widely recognized, the rejection is directed to the lack of adequate written description and not lack of an enabling disclosure. Even with such advances, the state of the art still does not allow one of skill in the art to predict the structure and function of a naturally-occurring variant of a polypeptide based solely on a single disclosed amino acid sequence - see for example, Brenner (*Trends in Genetics* 15:132-133), Seffernick et al., and Scott et al. as described above. Most importantly, one skilled in the art would not be able to divine the function(s) of other naturally-occurring protein sequences based on the knowledge of the asserted kinase function of only one disclosed species. For inventions in an unpredictable art, adequate written description of a genus that embraces widely variant species cannot be achieved by disclosing only one species within the genus.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 3 is rejected under 35 U.S.C. 102(b) as being anticipated by GenBank Accession No. AA639414. The rejection is explained in the previous Office Action.

Applicants argue that as amended the claims recite nucleic acids either encoding 150 contiguous amino acids or 500 contiguous nucleotides. However, it is noted that Claim 3 still includes polynucleotides which encode a polypeptide comprising an immunogenic fragment of SEQ ID NO:5. The polynucleotide of GenBank Accession No. AA639414 would encode amino acids 329-384 of SEQ ID NO:5 which clearly would be an immunogenic fragment thereof.

Claim 3 is are rejected under 35 U.S.C. 102(a) as being anticipated by GenBank Accession No. AI042283. The rejection is explained in the previous Office Action.

Claims 3, 5, 6, 8, 10 and 11 are rejected under 35 U.S.C. 102(a) as being anticipated by Young et al. (WO98/54963). The rejection is explained in the previous Office Action.

Claims 3, 5, 6, and 8 are rejected under 35 U.S.C. 102(a) as being anticipated by Kohama et al. The rejection is explained in the previous Office Action.

Applicants argue that each of above the rejections under 35 U.S.C. 102(a) should be withdrawn as Reference No. 11 submitted by applicant evidences a date of invention by applicants prior to the publication date of GenBank Accession No. AI042283, Young et al. and Kohama et al. However, this is not persuasive as any evidence of prior invention must be submitted in a declaration under 37 C.F.R 1.131. Furthermore, the page submitted as reference 11 by applicants, even if submitted within a 1.1.31 declaration would be insufficient to antedate the cited references as the page shows no sequence or anything that can be correlated to the nucleic acid of SEQ ID NO:19 disclosed in the instant application.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that

was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kohama et al. in view of GenBank Accession Nos. D31133, AA232791, W63556, AA081152, and AA026479. The rejection is explained in the previous Office Action.

Applicant traverses this rejection by arguing that Kohama et al. is not prior art as discussed above and that absent the disclosure of Kohama et al. the skilled artisan would not have any reason to combine the cited ESTs. However, this is not persuasive for the reasons discussed above. As such this rejection is maintained as well

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action

is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca Prouty, Ph.D. whose telephone number is (571) 272-0937. The examiner can normally be reached on Monday-Friday from 8:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. The fax phone number for this Group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Rebecca Prouty
Primary Examiner
Art Unit 1652